P7

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REMARKS

The above amendment to claims confirms changes agreed to by telephone with the Examiner. No new matter and no new issues of patentability are presented.

Applicants will submit formal drawings once the Notice of Allowability has been issued.

The Examiner has identified priority document information in the originally filed Declaration that needs to be updated. Applicants file herewith a newly executed Declaration and Power of Attorney. This new Declaration addresses the objections by the Examiner and complies with all Patent Office requirements.

Applicants submit herewith a paper copy of a Sequence Listing correcting the misnumbered amino acid residues. Please replace the originally filed Sequence Listing with the new Sequence Listing included herewith. Also enclosed is a Statement Under 37 C.F.R.

1.821(f), verifying that the sequence information in the enclosed paper copy is identical to the sequence information in the computer readable form originally filed.

If any further questions arise, the Examiner is invited to call the undersigned at (212) 415-8564.

Favorable reconsideration in view of the herewith presented amendment and remarks is respectfully requested.

It is believed that all of the pending claims are in condition for allowance. Early and favorable action by the Examiner is earnestly solicited.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for this response, or credit any overpayment to Deposit Account No. 13-4500, Order No. 2026-4149US4. A DUPLICATE COPY OF THIS SHEET IS ATTACHED.

Respectfully submitted,

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Dated: November 26, 2001

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VERSION WITH MARKINGS SHOWING CHANGES

IN THE CLAIMS

Please amend and replace the claims as follows:

23. (twice amended) A method of purifying [the autotaxin polypeptide of claim 26] an isolated autotaxin polypeptide comprising the steps of:

iii) collecting and concentrating supernatant from cultured cells whereby a first preparation of said polypeptide is produced;

iv) salt fractionating said first preparation to produce a second polypeptide preparation; and

isolating said polypeptide from said second preparation so that said polypeptide is obtained in substantially pure form, wherein the polypeptide comprises an amino acid sequence of human autotaxin having phosphodiesterase activity and cell motility-stimulating activity, wherein the polypeptide comprises the amino acid sequence N-Tyr-Met-Arg-Pro-Val-Tyr-Pro-Thr-Lys-Thr-Phe-Pro-Asn-C, residues 201 through 213 of SEQ ID NO: 69.

26. (twice amended) An isolated polypeptide comprising an amino acid sequence of human autotaxin having phosphodiesterase activity and cell motility-stimulating activity, wherein the polypeptide comprises the amino acid sequence [5'-] N-Tyr-Met-Arg-Pro-Val-Tyr-Pro-Thr-Lys-Thr-Phe-Pro-Asn-C [3'], residues 201 through 213 of SEQ ID NO: 69.

27. (amended) The isolated [peptide] polypeptide according to claim 26, wherein the polypeptide [is from about] comprises 788 amino [acids to about 979 amino acids in size] acid residues.

IN THE SPECIFICATION

Please replace the paragraph on page 1, lines 6-16 with the following:

> The present invention relates, in general, to a motility stimulating protein and compositions comprising the same. In particular, the present invention relates to a purified form of the protein and peptides thereof, for example, autotaxin (herein alternative referred to as "ATX"); a DNA segment encoding autotaxin; recombinant DNA molecules containing the DNA segment; cells containing the recombinant DNA molecule; a method of producing autotaxin; antibodies to autotaxin; and methods of cancer diagnosis and therapy using the above referenced protein or peptides thereof and DNA segments.

Please delete and replace the paragraph on page 14, line 26 through page 15, line 1 with the following:

> The present invention also relates to a DNA segment coding for a polypeptide comprising an amino acid sequence corresponding to ATX, or a unique portion of such a sequence (unique portion being defined herein as at least 5, 10, 25, or 50 amino acids). In one embodiment, the DNA segment encodes any one of the amino acid sequences shown in SEQ ID NO:1 to SEQ ID NO:11 and SEQ ID NO:26 to SEQ ID NO:33. Another embodiment uses larger DNA fragments encoding amino acid sequences shown in SEQ ID NO:34, SEQ ID NO: 36 and SEQ ID NO: [38] 70. The entire coding region for autotaxin can also be used in the present invention shown in SEQ ID NO:66 through SEQ ID NO:69.

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Please delete and replace the paragraphs on page 38, line 30 through page 39, line 25 with the following:

> A reverse transcriptase reaction was performed using total or oligo-(dT) purified RNA from A2058 or N-tera 2D1 cells as template and an anti-sense primer from the 5' end of 4C11 (GCTCAGATAAGGAGGAAAGAG; SEQ ID NO: 55). This was followed by one or two PCR amplification of the resultant cDNA using the commercially available kit from Perkin-Elmer and following manufacturer's directions. These PCR reactions utilized nested antisense primers from 4C11 (GAATCCGTAGGACATCTGCTT; SEQ ID NO: 56 and TGTAGGCCAAACAGTTCTGAC; SEQ ID NO: 57) as well as degenerate, nested sense primers deduced from ATX peptides: ATX-101 (AAYTCIATGCARACIGTITTYGTIG; SEQ ID NO: 58 and TTYGTIGGITAYGGICCIACITTYAA; SEQ ID NO: 59), ATX-103 (AAYTAYCTIACIAAYGTIGAYGAYAT; SEQ ID NO: 60 and GAYGAYATIACICTIGTICCIGGIAC; SEQ ID NO: 61), or ATX-224 (TGYTTYGARYTICARGARGCIGGICCICC; SEQ ID NO: 62). The amplified DNA was then purified from a polyacrylamide gel using standard procedures and ligated into the pCR™ plasmid using the TA cloning kit (Invitrogen Corporation) according to manufacturer's directions.
>
> The 5' RACE kit was utilized to extend the 5' end of ATX cDNA using total RNA from N-tera 2D1 as template and previously obtained sequence as primer (GCTGTCTTCAAACACAGC; SEQ ID NO: 63). The 5' end of the A2058 synthesized protein was obtained by using previously obtained sequence as primer

(CTGGTGGCTGTAATCCATAGC; SEQ ID NO: 64) in a reverse transcriptase reaction with total A2058 RNA as template, followed by PCR amplification utilizing the 5' end of N-tera 2D1 sequence as sense primer (CGTGAAGGCAAAGAGAACACG; SEQ ID NO: 65) and a nested antisense primer (GCTGTCTTCAAACACAGC; SEQ ID NO: 63). A2058 DNA encoding ATX is set forth in a SEQ ID NO:68 and the amino acid sequence is provided in SEQ ID NO:69.

Please delete and replace the following paragraph on page 40, lines 25-36 with the following:

The 5′ end of ATX has proven difficult to obtain from either tumor cell line to date. Normal human liver mRNA was therefore amplified using the 5′ RACE kit (Clontech) with known sequence from A2058 ATX as antisense primer. A DNA segment was obtained and has been sequenced. This segment codes for 979 amino acids, including an initiating methionine (SEQ ID NO:[38] 70). The putative protein sequence also includes a 20 amino acid transmembrane domain which is different from the tumor ATX's (SEQ ID NO:54), as shown in Table 7. Both tumorous forms of ATX apparently lack a transmembrane region and are instead secreted proteins.